

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) 8322-3 PAR

Box No. I TITLE OF INVENTION

PEPTIDES FOR TREATMENT OF INFLAMMATION AND SHOCK

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

UNIVERSITY TECHNOLOGIES INTERNATIONAL INC.

Suite 204, 609 - 14 Street NW
Calgary, Alberta, Canada
T2N 2A1

 This person is also inventor.Telephone No.
(403) 270-7027Facsimile No.
(403) 270-2384

Teleprinter No.

State (i.e. country) of nationality:
CAState (i.e. country) of residence:
CAThis person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

MATHISON, Ronald
208 Silverhill Crescent NW
Calgary, Alberta, Canada
T3B 3Y3

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)State (i.e. country) of nationality:
CAState (i.e. country) of residence:
CAThis person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of: Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

 agent common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

RAE, Patricia
Sim & McBurney
330 University Avenue, 6th Floor
Toronto, Ontario, Canada
M5G 1R7

Telephone No.
(416) 595-1155Facsimile No.
(416) 595-1163

Teleprinter No.

 Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box 3. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation
The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

DAVISON, Joseph S.
 600 Dalmeny Hill NW
 Calgary, Alberta, Canada
 T3A 1R3

This person is:

- applicant only
- applicant and inventor
- inventor only (*If this check-box is marked, do not fill in below.*)

State (i.e. country) of nationality:
CAState (i.e. country) of residence:
CA

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Name and address: (Family name followed by given name; for a legal entity, full official designation
The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

BEFUS, Dean
 14015 Valleyview Drive
 Edmonton, Alberta, Canada
 T5R 5T9

This person is:

- applicant only
- applicant and inventor
- inventor only (*If this check-box is marked, do not fill in below.*)

State (i.e. country) of nationality:
CAState (i.e. country) of residence:
CA

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Name and address: (Family name followed by given name; for a legal entity, full official designation
The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

MOORE, Graham
 1762 1A Avenue NW
 Calgary, Alberta, Canada
 T2N 0B2

This person is:

- applicant only
- applicant and inventor
- inventor only (*If this check-box is marked, do not fill in below.*)

State (i.e. country) of nationality:
CAState (i.e. country) of residence:
CA

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Name and address: (Family name followed by given name; for a legal entity, full official designation
The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

- applicant only
- applicant and inventor
- inventor only (*If this check-box is marked, do not fill in below.*)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGN ON OF STATES

The following designations are hereby made under Rule 4.9(a) (*mark the applicable check-boxes; at least one must be marked*):

Regional Patent

- AP ARIPO Patent: KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (*if other kind of protection or treatment desired, specify on dotted line*)

National Patent (*if other kind of protection or treatment desired, specify on dotted line*):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakstan | |
| <input checked="" type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |
| <input checked="" type="checkbox"/> LR Liberia | |
| <input checked="" type="checkbox"/> LS Lesotho | |
| <input checked="" type="checkbox"/> LT Lithuania | |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- ZW Zimbabwe
- SL Sierra Leone
- GH Ghana
- YU Yugoslavia

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (*Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.*)

Box No. VI PRIORITY CLAIMFurther priority claims are indicated in the Supplemental Box

The priority of the following earlier application(s) is hereby claimed:

Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1) GB	13 August 1996 (13-08-96)	9617021.2	
item (2)			
item (3)			

Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):

The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): ISA/

Earlier search Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:

Country (or regional Office): Date (day/month/year): Number:

Box No. VIII CHECK LIST

This international application contains the following number of sheets:	This international application is accompanied by the item(s) marked below:	
1. request : 5 sheets	1. <input type="checkbox"/> separate signed power of attorney	5. <input checked="" type="checkbox"/> fee calculation sheet
2. description : 30 sheets	2. <input type="checkbox"/> copy of general power of attorney	6. <input type="checkbox"/> separate indications concerning deposited microorganisms
3. claims : 3 sheets	3. <input type="checkbox"/> statement explaining lack of signature	7. <input type="checkbox"/> nucleotide and/or amino acid sequence listing (diskette)
4. abstract : 1 sheets	4. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s):	8. <input type="checkbox"/> other (specify):
5. drawings : 15 sheets		
Total : 54 sheets		

Figure No. 11 of the drawings (if any) should accompany the abstract when it is published.

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Patricia A. Rae
Sim & McBurney

For receiving Office use only		2. Drawings <input type="checkbox"/> received: <input type="checkbox"/> not received:
1. Date of actual receipt of the purported international application:		
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority specified by the applicant:	ISA/	

— For International Bureau use only —

Date of receipt of the record copy by the International Bureau:

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
 Sim & McBurney
 Attn. RAE, Patricia
 330 University Avenue
 6th floor
 Toronto, Ontario M5G 1R7
 CANADA

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

To: Sim & McBurney Attn. RAE, Patricia 330 University Avenue 6th floor Toronto, Ontario M5G 1R7 CANADA	Date of mailing (day/month/year) 06.02.98
Applicant's or agent's file reference 8322-3 PAR	PAYMENT DUE within 45 100 days from the above date of mailing
International application No. PCT/CA 97/00568	International filing date (day/month/year) 13/08/1997
Applicant UNIVERSITY TECHNOLOGIES INTERNATIONAL INC. et al.	

1. This International Searching Authority

- (i) considers that there are 3 (number of) inventions claimed in the international application covered by the claims indicated ~~below~~ on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~ on the extra sheet:

- (ii) has carried out a partial international search (see Annex) will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:
2-6, 9, 10; 1, 8, 12-20 in part
- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:

$$\underline{\text{DEM } 2200,-} \quad \times \quad \underline{2} \quad = \quad \underline{\text{DEM } 4400,-}$$

Fee per additional invention number of additional inventions total amount of additional fees

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. Claim(s) Nos. See attached sheet (third page) have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Véronique Baillou 
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1. Claims: 2-6, 9, 10; 1, 8, 12-20 in part

Peptides of claims 2-6, and subject-matter relating to said peptides.

The present application does not comply with the requirements of unity of invention [Rule 13(1) PCT]. At least 3 separate inventions have been identified. Each of them is characterised by an individual "special technical feature"; there is no technical interrelation between these inventions (see below). The applicants are therefore asked to pay additional search fees. Otherwise the International Search Report will be limited to the first invention specified below [Rule 40 PCT; Art. 17(3)(a) PCT].

Searched:

1st: Claims 2-6, 9, 10; 1, 8, 12-20 in part: peptides of claims 2-6, and subject-matter relating to said peptides.

Not yet searched:

2nd: Claims 11; 12-20 in part: the peptide of claim 11, and subject-matter relating to it.

3rd-nth: Claims 1, 7, 8, 12-20 in part: Other peptides of claim 1, and subject-matter relating to said peptides.

NOTE: Formula 1 covers a vast range of structurally almost unrelated peptides; it can be assumed that thousands of peptides correspond to the vague criteria of claim 1. Therefore, applicants are asked to indicate themselves substructures (= putative invention(s)) which are linked by a unifying non-trivial structural feature. One search fee will be due for each invention. Simple payment for this item, without indication of the structure(s) to be searched will result in further non-unity objections, and/or an incomplete search.

The following arguments reflect the preliminary opinion of the ISA concerning unity of invention:

1). Rule 13(2) PCT demands that "Rule 13.1 PCT shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression 'special technical features' shall mean those technical features which define a contribution which each of the claimed invention considered as a whole makes over the prior art."

The Administrative Instructions under the PCT, Annex B(f)(v) state that "if it can be shown that at least one Markush alternative is not novel, unity of invention should be re considered", and the PCT Preliminary Examination Guidelines C-III 7.6 say that "if the common matter of the independent claim is well known, and the remaining subject-matter ... differs without there being any unifying novel concept common to all of them, then clearly there is lack of unity".

1.1. As outlined in the description, the problem underlying the present application is to provide peptide with anti-anaphylactic (-endotoxic, -inflammatory) activity.

1.2. The solution to this problem in its broadest form is represented by the general formula of claim 1.

1.3. A vague general formula as such is not regarded as the unifying concept. A novel and non-obvious "special technical feature" must be common to all embodiments falling under that formula.

NOTE that the compound of claim 11 does not even correspond to the vague structural criteria of claim 1.

1.4. Even for the restricted scope of the first invention, several compounds have been retrieved that destroy the novelty of a preferred range of compounds, see all "X" citations of the preliminary international search report.

It follows that the vague structural features of claim 1 cannot be used to motivate unity of invention.

1.5. Short anti-anaphylactic peptides with structural features that overlap with the scope of claim 1 (especially if seen together with the compound of claim 11!) are known, see for example the general claim of WO-A-92/11858. The concept "short anti-anaphylactic peptides" can thus not be used to motivate unity of invention.

[Moreover, the structural formula of claims 1 overlaps with classes of peptides which are distinguished by completely different biological activities, see for example Enkephalin derivatives (cf. as an example the compound H-2890, and page 203 of the BACHEM citation). It is therefore not credible that all compounds covered by claim 1 can have the same biological activity.]

1.6. The submandibular glands have been discussed for years as the origin of factors that downregulate neutrophil function. The origin of the peptides can thus not be used to motivate unity of invention, see Comp. Biochem. Physiol. vol 106C, page 44.

2). Please note also that Rule 13 PCT has a regulatory function (to prevent unjustified saving of fees and to ensure ready comprehensibility). Also from this more pragmatic approach the present application lacks unity of invention:

First, due to the lack of constant characteristic structural elements, competitors cannot inform themselves readily on the existing situation regarding protective rights.

Second, the equitable levying of fees has to be respected. Because of its heterogeneous content, the present application entails a far greater than average expense in the procedure up to grant (keep in mind that there is an ample background concerning compounds of related structure and function, thus necessitating several independent searches of restricted scope).

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

Claims Nos.: 13-18

because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Remark : Although claims 13-18 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/CA 97/00568

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
- 1-6, 8-10, 12-20
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.
3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 92 11858 A (ABBOTT LABORATORIES) 23 July 1992 * claim 1, claim 11; pages 1-4 * ---	1-6, 8-10, 12-20
Y	MATHISON, R. ET AL.: "Neural regulation of neutrophil involvement in pulmonary inflammation" COMP. BIOCHEM. PHYSIOL., vol. 106c, no. 1, 1993, page 39-48 XP002051005 * page 44-45, chapter "Submandibular gland ..." *	1-6, 8-10, 12-20
X	"Bachem Feinchemikalien AG, Hauptstrasse 144, CH-4416 Bubendorf/Switzerland:" BACHEM CATALOG S13, 1993, page 203 and 533 XP002051006 * compounds H-2585, H-2590; H-5125 and page 533 in general *	1,3,7-9
A	---	1-6, 8-10, 12-20
X	ABDERHALDEN, E. ET AL.: "Über das Verhalten von Tetrapeptiden ..." FERMENTFORSCHUNG, vol. 16, 1942, pages 98-114, XP002051007 * p. 99; p. 109, p. 11 *	1,3,7,8
	---	-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/CA 97/00568

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>SLOOTSTRA, J.W.: "Structural aspects of antibody-antigen interaction ..." MOLECULAR DIVERSITY, vol. 1, 1996, pages 87-96, XP002051008 * figs 2-4 *</p> <p>---</p>	1-4,6-8
P,X	<p>MATHISON, R.D. ET AL.: "Submandibular glands: novel structures ..." CAN. J. PHYSIOL. PHARMACOL., vol. 75, 1997, pages 407-413, XP002051009 * whole disclosure *</p> <p>-----</p>	1-5,7,8, 12-20

Patent Family Annex

Information on patent family members

International Application No

PCT/CA 97/00568

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9211858 A	23-07-92	US 5386011 A AT 148891 T CA 2095359 A DE 69124705 D EP 0564588 A JP 6504055 T	31-01-95 15-02-97 28-06-92 27-03-97 13-10-93 12-05-94